

What is claimed is:

1. An improved method for detecting and enumerating rare cells in a mixed cell population by obtaining a blood specimen from a test subject, said specimen comprising a mixed cell population suspected of containing said rare cells, which method comprises preparing an immunomagnetic sample wherein said blood specimen is mixed with magnetic particles coupled to a ligand which reacts specifically with a determinant of said rare cells, to the substantial exclusion of other sample components, contacting said immunomagnetic sample with at least one reagent which labels said determinant of said rare cells, and analyzing said labeled rare cells to determine the presence and number of any said rare cells in said immunomagnetic sample, wherein the greater the number of said rare cells present in said sample, the greater the severity of a disease state, and wherein the improvement comprises the addition of two or more fluorescently distinct sets of stabilized cell populations, permeabilized, for use as a range of control cells in said method, and wherein the membranes of said control cells are detectably labeled, and wherein said control cells contain stabilized cellular components and antigenic moieties of said control cells stabilized for a period up to six months by exposure to fixative.
2. The improved method of claim 1, wherein said rare cell is a cancer cell and said disease state is cancer.
3. The improved method of claim 1, wherein said control cells have determinants in common with said rare cells.
4. The improved method of claim 1, wherein said stabilized cell populations are selected from the group consisting of cell number, antigen density, and cell size.
5. The improved method of claim 1, wherein said addition of two or more fluorescently distinct sets of stabilized cell populations are external control cells.
6. The improved method of claim 1, wherein said addition of two or more fluorescently distinct sets of stabilized cell populations are internal control cells.
7. The improved method of claim 1, wherein said stabilized cells are redundantly labeled

with at least two distinct fluorescent labels having the same spectral properties.

8. The improved method as claimed in claim 1, wherein said membrane label is selected from the group consisting of long chain lipophilic carbocyanines, long chain lipophilic indocarbocyanines, long chain lipophilic indodicarbocyanines, and analogs thereof,
5 lipophilic aminostyryl dyes, and long chain analogs of C18 rhodamine B and C18 fluorescein dyes.
9. The improved method as claimed in claim 1, wherein said ligand is an anti-EpCam, and said reagent labels an intracellular cytokeratin, said EpCam and said cytokeratin being present in both said rare cell and said control cell.
10. The improved method as claimed in claim 1, wherein the control cell is an SKBR3 breast cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of mammoglobulin, human milk fat globulin, and HER-2/neu.
11. The improved method as claimed in claim 1, wherein the control cell is a MCF-7 breast cancer cell, further comprising a second detectably labeled surface determinant which is
15 an estrogen receptor.
12. The improved method as claimed in claim 1, wherein the control cell is an LNCaP prostate cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of PSMA, PSA, and androgen receptor.
13. The improved method as claimed in claim 1, wherein the control cell is a CEM T-cell
20 leukemia cancer cell, further comprising a second detectably labeled surface determinant which is a CD4 molecule.
14. The improved method as claimed in claim 1, wherein the control cell is a C32 melanoma cancer cell, further comprising a second detectably labeled surface determinant which is a CD146 molecule.
- 25 15. An improved kit for screening a patient sample for the presence of circulating tumor cells, said kit having coated magnetic nanoparticles with a magnetic core material, a protein base coating material, and an anti-EpCAM coupled, directly or indirectly, to said base coating material, at least one antibody having binding specificity for a cancer cell

determinant, and cell specific dye for excluding sample components other than said tumor cells from analysis, wherein the improvement comprises the addition of two distinct sets of stabilized cell populations, permeabilized, for use as control cells in said kit, said distinct sets of stabilized control cell populations having determinants in common with said rare cells, wherein said membranes of said control cells are detectably labeled, and cellular components and antigenic moieties of said control cells have been stabilized up to six months, said stabilized control cells being suspended in a buoyant density medium

5 16. The improved kit as claimed in claim 15, wherein said stabilized cells are used as an internal control.

10 17. The improved kit as claimed in claim 15, wherein said stabilized cells are used as an external control.

18. The improved kit as claimed in claim 15, wherein said buoyant density medium is histopack.

15 19. The improved kit as claimed in claim 15, wherein the control cell is a SKBR3 breast cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of mammoglobulin, human milk fat globulin, and HER-2/neu.

20. The improved kit as claimed in claim 15, wherein the control cell is a MCF-7 breast cancer cell, further comprising a second detectably labeled surface determinant which is an estrogen receptor.

20 21. The improved kit as claimed in claim 15, wherein the control cell is an LNCaP prostate cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of PSMA, PSA, and androgen receptor.

25 22. The improved kit as claimed in claim 15, wherein the control cells are C32 melanoma cancer cells, further comprising a second detectably labeled surface determinant which is a CD146 molecule.